Identification of miRNA Signatures during the Differentiation of hESCs into Retinal Pigment Epithelial Cells.

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Public Summary:
It has been proposed that human stem cell-derived retina-pigment epithelial (RPE) cells would be useful to replace dynfunctional RPE cells in patients with age-related macular degeneration. In this study, we have defined unique expression pattern for a family of genes encoding small RNAs during stem cell differentiation into (RPE) cells. We found that the up- or down-regulation of these small RNAs is correlated with the emergence and maturation of RPEs from cultured human stem cells. Because these small microRNAs (or miRNAs)are involved in gene transcription and protein translation, they are useful to modulate the cell development process. Our study suggests that these unique miRNA expression pattern would be useful to design experiments to promote and characterize RPE cell differentiation from human pluripotent stem cells.

Scientific Abstract:
Retinal pigment epithelium (RPE) cells can be obtained through in vitro differentiation of both embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs). We have previously identified 87 signature genes relevant to RPE cell differentiation and function through transcriptome analysis of both human ESC- and iPSC-derived RPE as well as normal fetal RPE. Here, we profile miRNA expression through small RNA-seq in human ESCs and their RPE derivatives. Much like conclusions drawn from our previous transcriptome analysis, we find that the overall miRNA landscape in RPE is distinct from ESCs and other differentiated somatic tissues. We also profile miRNA expression during intermediate stages of RPE differentiation and identified unique subsets of miRNAs that are gradually up- or down-regulated, suggesting that dynamic regulation of these miRNAs is associated with the RPE differentiation process. Indeed, the down-regulation of a subset of miRNAs during RPE differentiation is associated with up-regulation of RPE-specific genes, such as RPE65, which is exclusively expressed in RPE. We conclude that miRNA signatures can be used to classify different degrees of in vitro differentiation of RPE from human pluripotent stem cells. We suggest that RPE-specific miRNAs likely contribute to the functional maturation of RPE in vitro, similar to the regulation of RPE-specific mRNA expression.